REMARKS

Applicant expresses his appreciation to the Examiner for conducting a telephone interview on Feb. 25, 2004. During the interview, Applicant discussed with the Examiner the patentability issues raised by the Examiner in the Office Action. Claims 1, 12-14 and 21 have been amended. Claims 1-21 are now pending.

I. Objection to the Specification

The Specification was objected to for containing typos and some informalities as SEQ ID NOs. Applicants amend the Specification according to the Examiner's suggestion. Withdrawal of the objection is therefore respectfully requested.

II. Objection to the Abstract

The Abstract was objected to for containing a misspelled "proteings". Applicants amend the Abstract to correct this term. Withdrawal of the objection is therefore respectfully requested.

III. Rejection Under 35 USC §112, First Paragraph

Claims 1-21 are rejected under 35 USC §112, First Paragraph for lack of adequate written description.

During the telephone interview, the Examiner suggested that the preambles of the claimed method and kit be amended to specify "a method (kit) for treating atopic dermatitis". Applicant amends independent claims 1 and 12 accordingly.

Applicant also amends independent claim 1 to specify that a "therapeutically effective amount of a composition comprising a MC148p" is administered to a patient having atopic dermatitis. Support for the claim languages appears, for example, in the Specification at page 14, line 31 and page 15, line 1.

In this application clinical evidence is disclosed to show that patients having atopic dermatitis (AT) but infected with Molluscum Contagiosum Virus (MCV) have clearing of the dermis around MCV papules. As described in the Specification (at page 5, lines 25-31, and page 5) and shown in Figures 5A and 5B, the dermis of the AD patient adjacent to the MCV papule

resembles the appearance of the dermis in normal, i.e., non-AD skin. In contrast, analysis of a biopsy taken concurrently from a similar area of AD **on the same patient** but remote from any MCV papule reveals that the skin manifests typical pathological characteristics of AD: dense, predominantly lymphohistocytic infiltrate admixed with eosinophils around the blood vessels of the superficial plexus, and around vessels of the papillae and those of the upper reticular dermis. Page 6, lines 1-5. Applicant believes that it is the MC148 protein encoded by MCV in the papule that exerts the therapeutic effects on AD in the patient.

Applicant' experiments further confirmed that an MC148P indeed can specifically target AD-relevant cells and inhibit chemotaxis of such cells stimulated by a specific ligand for CCR8. As described in more detail in Dr. David Paslin's declaration under 37 CFR §1.132, Applicant designed in vitro experiments involving cellular models of activated Th2 cells predominantly present in the skin of AD patients. Since the inflammatory response of AD is predominantly mediated via activated Th2 cells which express CCR8, Applicants used a CCR8-expressing cell line, 4DE4 pre-B lymphoma cells, which provide an experimental model comparable to the activated Th2 cells present in an AD patient's skin. Upon stimulation by a CCR8-specific ligand, I-309 (a β chemokine), chemotaxis occurs, mimicking the inflammatory response in AD skin. As shown in Dr. Paslin's declaration, a MC148P was able to inhibit effectively chemotaxis of the 4DE4 cells at IC_{50} of 2 nM. In comparison, the MC148P competed poorly (at IC_{50} of >150 nM) with the chemotaxis stimulated by SDF-1β, an α chemokine ligand for CXCR4. These results demonstrate that a MC148P can specifically inhibit chemotaxis of CCR8-expressing cells such as activated Th2 cells as found in AD skin, thereby further supporting the claimed method of using a MC148P to treat AD in a patient.

Pursuant to MPEP 2107.03, "if reasonably correlated to the particular therapeutic or pharmacological utility, data generated using *in vitro* assays, or from testing in an animal model or a combination thereof almost invariably will be sufficient to establish therapeutic or pharmacological utility for a compound, composition or process'. According to the MPEP and relevant case laws, courts have cautioned that

> Office personnel should not impose on applicants the unnecessary burden of providing evidence from human clinical trials. There is no decisional law that requires an applicant to provide data from human clinical trials to establish utility for an invention related to treatment of human disorders (see *In re Isaacs*, 347 F.2d 889, 146 USPQ 193 (CCPA 1963); *In re Langer*, 503 F.2d 1380, 183 USPQ

> 288 (CCPA 1974)), even with respect to situations where no art-recognized animal models existed for the human disease encompassed by the claims. *Ex parte Balzarini*, 21 USPQ2d 1892 (Bd. Pat. App. & Inter. 1991).

MPEP 2107.03.

Claim 1 as amended specifies that a "therapeutically effective amount of a composition comprising a MC148p" is administered to a patient having atopic dermatitis. Pursuant to MPEP 2173.05 (c),

> In *Ex parte Skuballa*, 12 USPQ2d 1570 (Bd. Pat. App. & Inter. 1989), the Board held that a pharmaceutical composition claim which recited an "effective amount of a compound of claim 1" without stating the function to be achieved was definite, particularly when read in light of the supporting disclosure which provided guidelines as to the intended utilities and how the uses could be effected.

The Specification of the instant application describes at length how a MC148P can be used for treating AD. For example, the Specification teaches that the MC148P may be formulated as an injectable solution and administered to an AD patient by injection intravenously, intramuscularly, subcutaneously or intradermally or by electroporation or iontophoresis. Page 3, lines 19-20; and pages 14-15.

Based on the amendments to the claims and the teaching of the specification, Applicant submits that claims 1-21 are supported by adequate written description. The therapeutic effect of MC148P claimed in the application is further supported by experimental evidence showing that MC148P can specifically inhibit chemotaxis of CCR8-expressing Th2 cells such as those in the skin of an AD patient. Withdrawal of the rejection under 35 USC §112, First Paragraph is therefore respectfully requested.

IV. Rejection Under 35 USC §112, Second Paragraph

Claims 1-21 are rejected under 35 USC §112, Second Paragraph for being indefinite. Applicant amended claims under the Examiner's guidance and therefore respectfully request withdrawal of this ground of the rejection.

V. Rejection Under 35 USC §102(b)

Claim 1 is rejected under 35 USC §102(b) as being anticipated by Krathwohl et al. (PNAS (1997) 94:9875-9880). Specifically the Examiner alleges that Krathwohl et al. teach a method comprising administering MC148R, a protein having the same structure as MC148 P of the instant application, to **patients suffering from atopic dermatitis**. Applicants respectfully traverse the Examiner's rejection based on the following reasons.

Claim 1 as amended specifies a method for treating a patient having atopic dermatitis by administering to the patient a therapeutically effective amount of a composition comprising a MC148P. Contrary to the Examiner's allegation, Krathwohl et al. disclosed a virological study of MCV which reveals that the viral chemokines encoded by MCV1 inhibits human hematopoietic progenitor cells. *See* Abstract. This evidence was used to support the authors' proposed the mechanism for escape of MCV from immune system surveillance. Page 9877, under "DISCUSSION". Nowhere in this cited reference is there a teaching or suggestion that the viral protein MC148P can be exploited for a **beneficial use** in humans, e.g., for treating patients with AD as claimed in the instant application.

VI. Rejection Under 35 USC §103(a)

1. Fife et al. in view of Untereker et al.

Claims 1-5 and 7-11 are rejected under 35 USC §103(a) as being unpatentable over Fife et al. (WO 99/09178) in view of Untereker et al . (US Patent No. 5,573,503).
The Examiner rejects the claims based on the rational that "Fife et al. teach the same function of the protein in the medicament for skin lesion, the same methods of administering the composition and similar pharmaceutically acceptable carriers". Applicants respectfully traverse the Examiner's rejection based on the following reasons.

As discussed in detail above, independent claim 1 as amended specifies a method for treating a patient having atopic dermatitis by administering to the patient a therapeutically effective amount of a composition comprising a MC148P.

In contrast, Fife et al. discloses the cloning and isolation of chemokine-like MCV protein. *See* "Claims" and "Summary of Invention". Based on this, Fife et al. further teaches in general

"a method for treating **MCV induced proliferative lesions of the skin** in an individual comprising **inhibiting the activity of chemokine-like MCV viral protein in the lesion**". Emphasis added, page 4, lines 8-11. Although Fife et al. also discloses a general method for inhibiting the action of human chemokines in a cell by administering a chemokine-like MCV viral protein (page 4, lines 23-25), there is only a "laundry list" of diseases that **might be** treated: asthma, Hodgkins disease, inflamed adenoids, tonsilitis, Epstein-Barr virus, pneumonia, myocarditis, rheumatoid arthristis and other autoimmune diseases. Page 11, lines 2-3. Nowhere in Fife et al. could be found a teaching or suggestion of a method of treating patients with AD using a viral protein MC148P as claimed in the instant application.

The secondary reference, Untereker et al., fails to supply the claim elements which are missing in Fife et al. but required for the establishment of a prima facie case of obviousness under 35 USC §103(a). As acknowledged by the Examiner, Untereker et al. merely teaches an ionophoretic drug delivery system. Thus, the cited references, each alone or in combination, fail to teach or suggest the claimed method. In view of the deficient teaching of the cited references Applicants submit that a prima facie case of obviousness has not been established, and respectfully request the withdrawal of the rejection under 35 USC §103(a).

2. Fife et al. in view of Untereker et al., and in further view of Fuisz

Claims 12-21 are rejected under 35 USC §103(a) as being unpatentable over Fife et al. in view of Untereker et al . and in further view of Fuisz (US Patent No. 5,733,269).

As discussed in detail above, Fife et al. and Untereker et al., each alone or in combination, fail to teach the claimed method for treating AD patient with a MC148P protein. The other reference cited, Fuisz, fails to supply the claim elements which are missing in both Fife et al. and Untereker et al. but required for the establishment of a prima facie case of obviousness under 35 USC §103(a). As acknowledged by the Examiner, Fuisz merely teaches a method and kit for a transdermal drug delivery system.

Thus, the three cited references, each alone or in combination, fail to teach or suggest the claimed kit. In view of this failure, Applicants submit that a prima facie case of obviousness has not been established, and respectfully request the withdrawal of the rejection under 35 USC §103(a).

CONCLUSION

In light of the amendments and arguments set forth above, Applicants earnestly believe that they are entitled to a letters patent, and respectfully solicit the Examiner to expedite prosecution of this patent to issuance. Should the Examiner have any questions, Examiner is encouraged to telephone the undersigned.

Respectfully,

WILSON SONSINI GOODRICH & ROSATI

Date: March 17, 2004 By: _____

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